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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/579,988 | 08/08/2006 | Warren J. Leonard | 252024 | 4910 |

45733 7590 07/14/2010

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| EXAMINER | |
|---|---|
| LEAVITT, MARIA GOMEZ | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1633 | |

| NOTIFICATION DATE | DELIVERY MODE |
|---|---|
| 07/14/2010 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Chgpatent@leydig.com

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/579,988 | LEONARD ET AL. | |
| | Examiner | Art Unit | |
| | MARIA LEAVITT | 1633 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *29 April 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *5,8,10-12,18,20 and 32-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,8,10-12,18,20 and 32-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04-29-2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

***Detailed Action***

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
2. Status of claims. Applicants' response of 04-29-2010 has been entered. Claims 5, 8, 10-12, 18, 20 and 32-35 are pending. Claims 5 and 18 have been amended by Applicants' amendment filed on 04-29-2010. Applicant's election of species: "a viral antigen' from the antigens recited in claim 11 was previously acknowledged. Applicant timely traversed the restriction (election) requirement in the reply filed on 05/02/2007.
3. The examiner acknowledges receiving an executed Declaration under 37 C.F.R. § 1.132 signed by Dr. Warren Leonard on April 04, 2010 ("Leonard Decl. "), and filed on 04-29-2010.
4. Therefore, claims 5, 8, 10-12, 18, 20 and 32-35 are currently under examination to which the following grounds of rejection are applicable.

***Response to arguments***

***Withdrawn objection/ rejection in response to applicants' amendments***

***Claim Rejections - 35 USC § 112- Second Paragraph***

In view of Applicants' amendment of independent claims 5 and 18, rejection of claims 5, 8, 10-12, 18, 20 and 32-35 under 35 U.S.C. 112, second paragraph has been withdrawn.

Applicants' arguments are moot in view of the withdrawn rejection.

***Rejections maintained in response to applicants' amendments***

***Claim Rejections - 35 USC § 103***

Claims 5, 8, 10-12, 18, 20 and 32-35 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Newell et al. (US Publication No. 2003/0138433, Publication Date July 3, 2003; hereafter referred to as "Newell"), in view of Novak et al (US Publication No. . 2003/0125524, of record; Publication date September 26, 2002; see SCORE search results for 10579988 and Search Result 20091207_124249_us-10-579-988a-1.rag.Results 3).

***Response to Applicants' Arguments as they apply to rejection of Claims 5, 8, 10-12, 18, 20 and 32-35 under 35 U.S.C. 103(a)***

At pages 6-9 of the remarks filed on 04-29-2010, Applicants essentially argue that: 1) the inventors discovered that IL-21 induces differentiation of human B cells into plasma cells an memory B cells as evidenced in Example 4, 2) prior to the inventors' discovery, one of ordinary skill in the art would not have recognized that contacting an isolated population of mature B cells and/or B cell progenitors with IL-21 would induce differentiation of memory B cells into plasma cells and memory B cells ( see paragraph 5 of the Leonard Decl.), 3) The Novak reference merely mentions that "[p]roteins of the present invention are useful for stimulating proliferation, activation, differentiation and/or induction or inhibition of specialized cell function of cells of the involved homeostasis of the hematopoiesis and immune function," wherein hematopoietic lineages include, but are not limited to, T cells, B ceils, NK cells, dendritic ceils, monocytes, macrophages, and epithelial cells (see paragraph 7 of the Leonard Decl.)', 4) Thus, one of ordinary skill in the art, upon reading the Novak reference, would not have recognized that that contacting isolated mature B cells and/or B cell progenitors with IL-21 would induce differentiation of the B cells into plasma ceils and memory B cells, 5) the Newell reference

merely discloses that a primary encounter with an antigen can stimulate specific B cells to differentiate into cells that produce antibody at a high rate (plasma cells) and populations of memory cells (see paragraph 9 of the of the Leonard Decl), 6) Thus, based on the disclosure of the Newell reference, one of ordinary skill in the art would not have recognized that contacting isolated mature B cells and/or B cell progenitors with a composition comprising IL-21 would induce differentiation of the B cells into plasma cells and memory B cells, and 7) neither of the cited references discloses isolating or purifying one or more of the memory B cell and the plasma cell (whose differentiation was induced by contacting mature B cells and/or B cell progenitors with IL-21) and introducing at least one of the memory B cell and the plasma cell into the subject, as required by the pending claims. The above arguments have been fully considered but deemed unpersuasive.

Regarding 1), 2), 3) and 5), Newell clearly discloses methods for promoting antigen-specific immune responses (page 1, paragraph [0003]) comprising obtaining B cells that have been originally isolated from a subject and subsequently contacted *in vitro* with a target antigen-conjugate to produce target antigen manipulated B cells. Additionally, Newell states that primary encounter with antigens stimulates specific B cells not only to differentiate into cells that produce antibody at a high rate (plasma cells), but also to give rise to populations of memory cells. Furthermore, Newell evidences in *vitro* contacting isolated B cells with cytokines (e., g, IL-2, TNF-α,and IFN-γ, IL-4, IL-5, IL-6, IL-9, IL-10, and IL-13) which provide optimal help for humoral immune responses such as IgE and IgG4 antibody isotype switching, high level antibody production (humoral immunity) by T-dependent B cell responses, promoting cell growth, inducing viral resistance and others. Thus cytokines explicitly contribute to

differentiation of mature B cells to antibody producing plasma cells Note that the instant invention encompass isolating a population of B cells (e.g., mature or progenitor) that differentiate upon contact with an antigen into memory B cells and plasma cells. Novak complements the teachings of Newell by disclosing a cytokine of 162 amino acids in lengthhaving 100% sequence homology to the polypeptide of SEQ ID NO: 1 of the claimed invention and useful for expansion, proliferation, activation, differentiation, and/or induction or inhibition of specialized cell including growth/expansion and/or differentiated state of B cells *in vivo*. So if contacting a population comprising an isolated mature B cell and a B cell progenitor with a cytokine and an antigen stimulates specific B cells to differentiate into plasma cells and memory B cells, contacting an isolated population comprising a mature B cell and a B cell progenitor with an isolated human cytokine of 162 amino acids in length, designated zalpha11 ligand should be reasonably expected to promote differentiation into plasma cells and memory cells for the same reason contacting with any of the cytokines IL-2, TNF-α,and IFN-γ, IL-4, IL-5, IL-6, IL-9, IL-10, and IL-13 promotes a mature B cell and a B cell progenitor to differentiate into plasma cells and memory cells – all compounds are cytokines having an effect on the growth/expansion and/or differentiated state of mature B cells. There is no evidence in the specification or of record beyond what Novak teaches for IL-21 and its affect on B-cells. Thus, all of the elements of the claims were known to one of ordinary skill in the art at the time the invention was made and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions and the combination would have yielded nothing more than predictable results to one of ordinary skill in the art at the time of invention. Where the unexpected properties of a claimed invention are not shown to have a

significance equal to or greater than the expected properties, the evidence of unexpected properties may not be sufficient to rebut the evidence of obviousness. *In re Nolan*, 553 F.2d 1261, 1267, 193 USPQ 641, 645 (CCPA 1977). "Expected beneficial results are evidence of obviousness of a claimed invention, just as unexpected results are evidence of unobviousness thereof." *In re Gershon*, 372 F.2d 535, 538, 152 USPQ 602, 604 (CCPA 1967). For the reasons set forth above, Applicants' arguments and the Leonard Decl. are not found persuasive. Based on the teachings in the prior art as a whole, one of skill in the art would have found the claimed invention *prima facie* obvious at the time the invention was made.

Regarding 4) and 6), in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). None of the references has to teach each and every claim limitation. If they did, this would have been anticipation and not an obviousness-type rejection.

Regarding 7), Newell unambiguously teaches obtaining B cells that have been originally isolated from a subject and *in vitro* contacting of the isolated B cells with an antigen and a Th2 cytokine(see ¶ [0015]; ¶ [0147] of the published application, for example). Though, Newell does not specifically teach purification of one or more memory B cell and the plasma cell after contacting with an antigen and a cytokine, Newell describes isolation and enrichment of mature B cells according to protocols well known in the art at the time the invention was made. Thus it would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to isolate mature B cells and/or B cell progenitors and/or memory B cells and/or

plasma cells with the expected beneficial results of separate the desired target cell for *ex vivo* treatment according to a methodology that was considered routine in the prior art.

***Conclusion***

Claims 5, 8, 10-12, 18, 20 and 32-35 are rejected.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria Leavitt whose telephone number is 571-272-1085. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Maria Leavitt/

Maria Leavitt
Primary Examiner, Art Unit 1633